

WHAT IS CLAIMED IS:

1. A method of treating a mammal having a disorder comprising insufficient cartilage growth or insufficient skeletal growth, the method comprising administering to the mammal an amount of a tumor necrosis factor-related activation induced cytokine (TRANCE)-inhibiting agent effective to increase cartilage growth or skeletal growth.

2. The method of claim 1, wherein the TRANCE-inhibiting agent is an antisense nucleic acid directed against a TRANCE RNA or a TRAF6 RNA.

3. The method of claim 2, wherein the antisense nucleic acid directed against a TRANCE RNA has the sequence of SEQ ID NO:17 or SEQ ID NO:18; and the antisense nucleic acid directed against the TRAF6 RNA has the sequence of SEQ ID NO:19.

4. The method of claim 2, wherein the antisense nucleic acid is administered locally at a site of insufficient cartilage growth or insufficient skeletal growth in the mammal.

5. The method of claim 1, wherein the disorder is selected from the group consisting of dwarfism, osteopetrosis, craniofacial-skeletal discrepancies, and bone or cartilage damage resulting from traumatic injury, surgery, osteoarthritis or rheumatoid arthritis.

6. The method of claim 1, wherein the TRANCE-inhibiting agent is a TRANCE-binding molecule that sequesters TRANCE to form an inactive complex.

7. The method of claim 6, wherein the TRANCE-binding molecule is an anti-TRANCE antibody, or a TRANCE-binding fragment thereof.

8. The method of claim 6, wherein the TRANCE-binding molecule is an isolated RANK receptor, or a TRANCE-binding fragment thereof.

9. A method of treating a mammal having a disorder comprising excessive cartilage growth or excessive skeletal growth, the method comprising administering to the mammal an

amount of a tumor necrosis factor-related activation induced cytokine (TRANCE)-increasing agent effective to decrease cartilage growth or skeletal growth.

10. The method of claim 9, wherein the TRANCE-increasing agent is a polypeptide comprising a tumor necrosis factor (TNF) domain of a TRANCE protein.

11. The method of claim 10, wherein the polypeptide is locally administered at a site of excessive cartilage growth or excessive skeletal growth in the mammal.

12. The method of claim 10, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, or SEQ ID NO:8, but lacks the cytoplasmic domain and transmembrane domain, of human TRANCE.

13. The method of claim 10, wherein the polypeptide consists of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 or SEQ ID NO:8.

14. The method of claim 10, wherein the TRANCE protein is human TRANCE protein.

15. The method of claim 9, wherein the TRANCE-increasing agent is a TRAF6 polypeptide.

16. The method of claim 15, wherein the TRAF6 polypeptide is a human TRAF6 polypeptide.

17. The method of claim 15, wherein the method comprises introducing a TRAF6 polypeptide into a chondrocyte at a site of excessive cartilage growth or excessive skeletal growth in the mammal.

18. The method of claim 17, wherein introducing the TRAF6 polypeptide into the chondrocyte comprises locally administering an expression vector comprising a nucleotide sequence encoding a TRAF6 polypeptide operably linked to an expression control sequence, whereby the expression vector enters the chondrocyte and expresses the TRAF6 polypeptide in the chondrocyte.

19. The method of claim 15, wherein: (a) the TRAF6 polypeptide is linked to a membrane translocation moiety to form a cell-permeating TRAF6, and (b) the cell-permeating TRAF6 is locally administered at a site of insufficient cartilage growth or insufficient skeletal growth in the mammal.

20. The method of claim 9, wherein the disorder is selected from the group consisting of acromegaly, gigantism, exostosis cartilaginea, exostosis bursata, and multiple osteochondilaginous exostoses.

21. A method of promoting growth of cartilage in a mammal, the method comprising: removing cartilage from a mammal; culturing the cartilage in vitro; contacting chondrocytes in the cartilage with a tumor necrosis factor-related activation induced cytokine (TRANCE)-inhibiting agent; and reintroducing the cartilage into the mammal.

22. The method of claim 20, wherein the TRANCE-inhibiting agent is a TRANCE antisense nucleic acid.

23. The method of claim 20, wherein the TRANCE-inhibiting agent is a TRAF6 antisense nucleic acid.

24. The method of claim 20, wherein the TRANCE-inhibiting agent is a TRANCE-binding molecule.

25. A method of diagnosing a cartilage disorder in a mammal, the method comprising

obtaining a chondrocyte from the mammal;

detecting a level of tumor necrosis factor-related activation induced cytokine (TRANCE), receptor activator of NF- κ B (RANK), or TNF-receptor-associated factor 6 (TRAF6) in the chondrocyte, wherein a level of TRANCE, RANK, or TRAF6 that is elevated or reduced compared to a normal level indicates the presence of a cartilage disorder in the mammal.

26. A method of identifying a candidate tumor necrosis factor-related activation induced cytokine (TRANCE)-inhibiting compound, the method comprising:

obtaining a cultured, proliferating test chondrocyte;

contacting the test chondrocyte with a test compound and a TRANCE polypeptide;

and

detecting proliferation in the test chondrocyte compared to a control chondrocyte contacted with a TRANCE polypeptide unaccompanied by the test compound, whereby an increase in proliferation indicates that the test compound is a candidate TRANCE-inhibiting compound.

27. The method of claim 26, wherein the chondrocyte is selected from the group consisting of: a primary chondrocyte, a chondrocyte from a cultured chondrocyte cell line, a primary chondrocyte from a TRANCE null, transgenic non-human mammal, and a chondrocyte from a cultured chondrocyte cell line derived from a TRANCE null, transgenic non-human mammal.

28. A method of identifying a candidate tumor necrosis factor-related activation induced cytokine (TRANCE)-increasing compound, the method comprising:

obtaining a cultured, proliferating test chondrocyte;

contacting the test chondrocyte with a test compound and a TRANCE polypeptide;

and

detecting proliferation in the test chondrocyte compared to a control chondrocyte contacted with a TRANCE polypeptide unaccompanied by the test compound, whereby a

decrease in proliferation indicates that the test compound is a candidate TRANCE-increasing compound.

29. The method of claim 28, wherein the chondrocyte is selected from the group consisting of: a primary chondrocyte, a chondrocyte from a cultured chondrocyte cell line, a primary chondrocyte from a TRANCE null, transgenic non-human mammal, and a chondrocyte from a cultured chondrocyte cell line derived from a TRANCE null, transgenic non-human mammal.